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## SYMPOSIUM

# The influence of pre-deployment neurocognitive functioning on post-deployment PTSD symptom outcomes among Iraq-deployed Army soldiers

BRIAN P. MARX,<sup>1,2,3</sup> SUSAN DORON-LAMARCA,<sup>1,2,3</sup> SUSAN P. PROCTOR,<sup>2,4,5</sup> AND JENNIFER J. VASTERLING<sup>1,2,3</sup>

<sup>1</sup>VA Boston Healthcare System, Behavioral Science Division, National Center for PTSD, Boston, Massachusetts

<sup>2</sup>Department of Psychology, VA Boston Healthcare System, Boston, Massachusetts

<sup>3</sup>Department of Psychiatry, Boston University School of Medicine, Boston, Massachusetts

<sup>4</sup>Military Performance Division, U.S. Army Research Institute of Environmental Medicine, Natick, Massachusetts

<sup>5</sup>Department of Environmental Health, Boston University School of Public Health, Boston, Massachusetts

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## Abstract

This study evaluated associations between pre-deployment neurocognitive performance and post-deployment posttraumatic stress disorder (PTSD) symptoms in a sample of deployed active duty Army soldiers. As part of a larger longitudinal study, each participant completed baseline measures of memory, executive attention, and response inhibition, and baseline and post-deployment self-report measures of PTSD symptom severity. Data were subjected to multiple regression analyses that examined associations between baseline neurocognitive performances and longitudinal PTSD symptom outcome. Results revealed that pre-trauma immediate recall of visual information was associated with post-deployment PTSD symptom severity, even after controlling for pre-deployment PTSD symptom levels, combat intensity, age, gender, and test-retest interval. There was also an interaction between pre-deployment PTSD symptom severity and pre-deployment immediate visual recall and verbal learning, indicating that neurocognitive performances were more strongly (and negatively) associated with residualized post-deployment PTSD symptoms at higher levels of pre-deployment PTSD symptoms. These findings highlight the potential role of pre-trauma neurocognitive functioning in moderating the effects of trauma exposure on PTSD symptoms. (*JINS*, 2009, *15*, 840–852.)

**Keywords:** Visual memory, Verbal memory, Attention, Neurocognitive functioning, PTSD, Combat

## INTRODUCTION

Neuroimaging studies of posttraumatic stress disorder (PTSD) suggest that PTSD is associated with functional and structural abnormalities in brain regions (e.g., prefrontal cortex, hippocampus, amygdala) relevant to fear and related emotions (Bonne, Grillon, Vythilingam, Neumeister, & Charney, 2004; Rasmusson, Vythilingam, & Morgan, 2003; Southwick, Rasmusson, Barron, & Arnsten, 2005; Yehuda, 2002). Correspondingly, an emerging literature examining

neuropsychological and information processing correlates of PTSD has revealed that PTSD in both military veterans and civilians is associated with cognitive abnormalities, particularly on tasks assessing learning, memory, and attention. Neuropsychological deficits appear to be circumscribed, with the most robust findings indicating impairment in acquiring new information (Gilbertson, Gurvits, Lasko, Orr, & Pitman, 2001; Jelinek, Jacobsen, & Kellner, 2006; Koenen et al., 2001), heightened sensitivity to interference on learning and memory tasks (Uddo, Vasterling, Brailey, & Sutker, 1993; Vasterling, Brailey, Constans, & Sutker, 1998; Vasterling et al., 2002; Yehuda et al., 1995), and impairment in working memory, inhibition, and other executive aspects of attention (Gilbertson et al., 2006; Jenkins, Langlais, Delis, & Cohen, 2000; Koenen et al., 2001; Leskin & White, 2007;

Correspondence and reprint requests: Brian P. Marx, Ph.D., National Center for PTSD (116B-2), VA Boston Healthcare System, 150 South Huntington Avenue, Boston MA 02130. E-mail: brian.marx@va.gov

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McFarlane, Weber, & Clark, 1993; Vasterling et al., 1998). Deficits in memory consolidation and shift of attention have also been observed. On experimental tasks using emotionally valenced stimuli, PTSD is associated with attentional and memory biases to threat-relevant information (e.g., Constans, McCloskey, Vasterling, Brailey, & Mathews, 2004; Dalgleish et al., 2003; Foa, Feske, Murdock, Kozak, & McCarthy, 1991; McNally, Kaspi, Riemann, & Zeitlin, 1990; McNally, Lasko, Macklin, & Pitman, 1995). Despite the vast gains in knowledge over the past decade regarding the neuropsychological correlates of PTSD, cross-sectional studies cannot address the direction of causation between neuropsychological compromise and PTSD. Although animal studies have suggested that stress may lead to neuropsychological compromise (Arnsten & Goldman-Rakic, 1998; Birnbaum, Gobeske, Auerbach, Taylor, & Arnsten, 1999; Ohl, Michaelis, Vollmann-Honsdorf, Kirschbaum, & Fuchs, 2000; Shansky et al., 2004), there is growing evidence that neurocognitive functioning may also serve as a risk/resilience factor for PTSD. Studies using archival pre-trauma estimates of general intellectual functioning derived from Army entrance examinations have generally revealed that the development of PTSD following trauma exposure is associated with lower pre-trauma estimates of intellectual functioning (e.g., Gale et al., 2008; Kremen, et al., 2007; Macklin et al., 1998), especially at lower levels of trauma exposure (Thompson & Gottesman, 2008).

Less is known, however, about the role that specific neurocognitive deficits, found to be commonly associated with PTSD (e.g., memory, inhibition, and attention deficits), play in either conferring risk or enhancing protection in developing PTSD following trauma. Using a sample of monozygotic twin pairs in which one twin was exposed to combat in Vietnam and the other was not, Gilbertson and colleagues found that twin pairs in which the exposed twin had PTSD showed smaller hippocampal volumes (Gilbertson et al., 2002) and performed more poorly on measures of attention, executive functioning, and verbal memory (Gilbertson et al., 2006) than twin pairs in which the exposed twin did not have PTSD. However, there were no significant differences in hippocampal volume or neurocognitive measures between brothers with PTSD and their nonexposed twins. Thus, hippocampal volume and neurocognitive functioning varied in part as a function of family membership, even when one brother had PTSD and the other did not. The results were interpreted to suggest that pre-exposure hippocampal volume and neurocognitive functioning may moderate the risk of developing PTSD following trauma exposure.

In a recent prospective investigation of civilian trauma survivors, Parslow and Jorm (2007) showed that more proficient pre-trauma performances on tasks of immediate and delayed verbal recall, verbal working-memory, visuomotor speed, and verbal intelligence were associated with lower post-trauma PTSD re-experiencing and arousal symptoms, with the strongest associations occurring in domains of immediate and delayed verbal recall, verbal intelligence, and working memory. The findings also revealed that participants

with high levels of post-trauma PTSD symptoms showed a more attenuated improvement (i.e., showed less practice effects) on a word recall task from pre- to post-deployment than participants with low levels of post-trauma PTSD symptoms. Overall, their findings provided evidence that cognitive deficits on a number of tasks conferred additional risk of developing PTSD symptoms, but also suggested that more circumscribed deficits in verbal learning may result from PTSD symptoms. Because the study did not assess PTSD symptom levels prior to the trauma exposure, the extent to which baseline neurocognitive functioning was associated with the development of new PTSD symptoms *versus* any pre-existing symptoms is unclear. In addition, because PTSD avoidance and numbing symptoms were not measured, the degree to which cognitive functioning was associated with the full range of PTSD symptoms is unknown.

Nonetheless, these findings, when combined with those of Gilbertson and colleagues, provide provocative evidence that certain neurocognitive functions, perhaps in particular those reflecting prefrontal and hippocampal functions (e.g., sustained attention, inhibitory functions, and immediate and delayed memory, respectively), possibly moderate the relationship between trauma exposure and PTSD symptom development. This is especially intriguing when viewed in the context of the potential interplay between cognitive skills, coping, and the encoding and subsequent retrieval of trauma memories, which are thought to be necessary for adequate psychological resolution of the trauma (Ehlers & Clark, 2000; Foa & Jaycox, 1999; Foa & Riggs, 1994). For example, it is possible that less proficient memory and attention compromises the initial encoding of the trauma, resulting in poorly elaborated and fragmented trauma narratives that then promote impaired retrieval of the trauma event. Likewise, it has been suggested that reduced cognitive ability to shift away from maladaptive cognitions or behaviors (Bremner et al., 2000; Shin et al., 2004) and decrements in the ability to gate or control trauma-related memories (Brewin, 2008; Vasterling & Brailey, 2005) may promote the development of PTSD.

The primary goal of this article was to use data prospectively gathered before and after exposure to extreme stress (i.e., Iraq War deployment) to test the hypothesis that the integrity at baseline of cognitive processes linked to memory and reflective of prefrontal and hippocampal functioning (i.e., initial acquisition of information, memory retention, sustained attention, inhibition, working memory) would be associated with PTSD symptom outcome following stress exposure. Using a unique set of neuropsychological and PTSD self-report data collected on a large sample of U.S. Army soldiers before and after they deployed to Iraq, we extended the methodology of Parslow and Jorm (2007) by assessing PTSD symptoms both prior to and after stress exposure and by measuring the full range of PTSD symptoms.

Although our primary hypotheses centered on longitudinal relationships between pre-deployment neurocognitive functioning and post-deployment levels of PTSD symptoms, we also sought to extend prior cross-sectional findings by examining associations between PTSD symptoms and concurrent

neurocognitive performances within a sample of active duty military personnel. This population extension facilitates examination of neurocognitive correlates of PTSD within a significantly briefer timeframe relative to stressor exposure than much of the prior research, in addition to allowing examination of a relatively healthy, nonclinically-recruited sample.

## METHODS

Human subjects approvals were obtained from Human Subjects Research Review Boards of the Army, Tulane University Health Sciences Center, and Department of Veterans Affairs. All participants provided written informed consent prior to participation.

### Participants

Participants were 668 active duty U.S. Army soldiers ( $n = 613$  men;  $n = 55$  women) deployed to Iraq between November 2003 and March 2005. These individuals were selected from 955 soldiers who deployed during the study period and who were enrolled in the Neurocognition Deployment Health Study (NDHS). Individuals were excluded from these analyses if they either did not perform the post-deployment assessment in person ( $n = 257$ ; 27%) or demonstrated invalid response profiles ( $n = 21$ ; 2%) or insufficient effort ( $n = 9$ ; 1%) at any of the assessments. The predominant reason for nonparticipation at the post-deployment assessment was relocation to another military installation characteristic of standard military duty rotation ( $n = 127$ ; 49%). Other reasons included separation from the military ( $n = 62$ ; 24%), leave or special assignments ( $n = 38$ ; 15%), declined participation ( $n = 7$ ; 3%), deployment at the time of assessment ( $n = 6$ ; 2%), illness ( $n = 3$ ; 1%), being deceased ( $n = 3$ ; 1%), and unknown or unconfirmed relocation ( $n = 11$ ; 4%).

### Measures

Comprehensive descriptions of primary assessment data and secondary data obtained from automated military databases are provided elsewhere (Vasterling et al., 2006a, 2006b). Measures relevant to this report follow.

#### *Demographic, neuromedical, and historical information*

Each assessment documented current demographic and military information (e.g., age, gender, rank), risk factors for neuropsychological disorders (e.g., history of neurodevelopmental disorders, psychiatric disorders, brain injury), and factors potentially affecting neuropsychological performance. Brain injury incurred during the course of the study was queried by interview and defined as any self-reported head injury resulting in at least momentary loss of consciousness. Self-reported ethnicity data were gathered to help gauge the representativeness of the sample.

#### *Performance-based neuropsychological tests*

In line with the hypotheses, which centered on the prospective association between pre-deployment levels of neurocognitive performance and post-deployment reports of PTSD symptom levels, analyses included tests of immediate and delayed verbal and visual memory, sustained attention, working memory, and inhibitory functioning. To assess learning and memory, participants completed the Wechsler Memory Scale, 3rd edition (WMS-III; Wechsler, 1997) Verbal Paired Associates and Wechsler Memory Scale (WMS; Wechsler, 1945) Visual Reproductions tasks. These tasks were chosen to measure memory processes in the verbal-auditory and visual-spatial modalities, respectively. Verbal Paired Associates includes four cued recall learning trials and a delayed cued recall condition. Visual Reproductions requires reproduction of simple geometric designs after a single exposure followed by a delayed recall condition. Learning was measured on the Verbal Paired Associates task as the sum of items correctly recalled over the four learning trials. Percent retention was calculated as delayed recall/immediate recall  $\times 100$  for Visual Reproductions and delayed recall/Trial D  $\times 100$  for Verbal Paired Associates.

To assess sustained attention and inhibition, participants completed the Neurobehavioral Evaluation System, 3rd edition (NES3) Continuous Performance Task (CPT; Letz, 2000), which requires detection of targets from distractor stimuli. Sustained attention impairment was measured by the number of omissions; disinhibition was measured by the number of false positive responses. All CPT error scores were log-transformed to adjust for nonnormal distributions. The NES3 vocabulary task was also administered to obtain an estimate of participants' IQ. The NES3 vocabulary task is a computer-assisted 25-item multiple-choice test designed to estimate general verbal ability (Letz, 2000) and is derived in part from the Armed Forces Qualifying Test – Verbal Subtest. Participants also completed the Trail Making Test, which assesses working memory and executive functioning (Reitan, 1958). Time to complete Part A (drawing lines between numerals in sequential order) was subtracted from time to complete Part B (drawing lines between sequential numbers and letters in alternation). The subtraction procedure parcels out basic attentional, psychomotor, and visual tracking skills, resulting in a better measure of working memory and cognitive flexibility.

All scores were free of subjective judgment except for Visual Reproductions, in which designs were scored by a primary rater according to set criteria. Reliability ratings performed on 10% of randomly selected drawings by a second rater blinded to unit and deployment status indicated high interrater reliability (Intraclass correlations: 0.75–0.95).

#### *Combat and PTSD symptom severity*

Combat severity was quantified by a modified version of the Deployment Risk and Resilience Inventory (DRRI; King, King, & Vogt, 2003) Combat Experiences module. The DRRI is a suite of self-report scales designed to assess risk



and resilience factors important to modern military deployments. Evidence is available for the internal consistency reliability, test-retest reliability, discriminant validity, discriminative validity, and criterion-related validity of DRRI scales (King, King, Vogt, Knight, & Samper, 2006). The Combat Experiences module of the DRRI yields a continuous score that indexes combat intensity, with higher scores indicating greater combat intensity.

The PTSD Checklist (PCL; Weathers, Litz, Herman, Huska, & Keane, 1993) is a 17-item self-report scale that assesses posttraumatic stress symptom severity, providing a summary score of overall PTSD symptom severity. Higher scores indicate greater symptom severity. The scale items correspond directly to *DSM-IV* (American Psychiatric Association, 1994) symptom criteria, measuring the reexperiencing, avoidance and emotional numbing, and hyperarousal symptoms of PTSD. This widely used instrument has demonstrated coefficient alphas greater than .95, is highly correlated with other measures of PTSD, including the "gold standard" Clinician-Administered PTSD Scale ( $r = .93$ ; Blake, Keane, Wine, & Mora, 1990), and has demonstrated acceptable levels of discriminant validity relative to measures of other forms of psychopathology (Blanchard, Jones-Alexander, Buckley, & Forneris, 1996; Forbes, Creamer, & Biddle, 2001; Ruggiero, Del Ben, Scotti, & Rabalais, 2003; Weathers et al., 1993).

### Response validity

Validity of response profiles on questionnaires was assessed via inspection of scales with bidirectional items (e.g., "5" endorses pathological functioning on some items and intact functioning on others). If a respondent provided all extreme responses in the same direction on a scale with bidirectional items, that respondent's data were not analyzed. The Test of Memory and Malinger (TOMM; Tombaugh, 1997) Trial 1 was administered to assess cognitive engagement. The data of participants scoring below 38, a cut-off found to show reasonable sensitivity and specificity in detecting insufficient effort on neurobehavioral tasks (O'Bryant, Engel, Kleiner, Vasterling, & Black, 2007), were excluded from analyses.

### Procedures

Participants completed paper-and-pencil survey and neuropsychological measures at both pre- and post-deployment assessments. Assessments were conducted at military installations by a civilian examiner team. All performance-based neuropsychological measures were individually administered according to scripted, standardized instructions. Participants completed paper-and-pencil surveys in small groups. Because soldiers participated in the study in a time of extraordinarily high operational demands, the study procedures were structured to optimize efficient use of their time, and the order of administration of the paper-and-pencil *versus* the neuropsychological tests was determined solely on the basis of immediate examiner availability and differed randomly across

participants. Tests included in the current analyses were drawn from the larger set of neuropsychological tests administered as part of the primary study.

### Statistical Analyses

Statistical analyses were performed using SPSS, v. 17.0. Descriptive statistics were computed for all study variables. When data distributions departed significantly from normal, raw scores were normalized via logarithmic transformation. Missing values for specific items on questionnaires were replaced by the mean value of the individual's completed items for that measure if the participant responded to at least 50% of the items. If less than 50% of the items on a measure were completed, summary scores were not computed. Outliers were truncated at 3 standard deviations (*SD*) from the mean.

To examine the prospective and cross-sectional associations between PTSD symptom severity and neuropsychological functioning, a series of hierarchical linear regression analyses were conducted. Because of the high collinearity between immediate recall and retention memory measures, we performed two separate regression analyses: (1) one that included only the measures of immediate visual and verbal memory, and (2) another that included only the measures of delayed (retention) visual and verbal memory.

To answer the primary question of whether deficits in pre-deployment neurocognitive performances would negatively predict post-deployment PTSD symptom scores after taking into account pre-deployment PTSD symptoms, we entered pre-deployment PCL scores in the first step. Based on previous research demonstrating that female gender (Breslau, Kessler, & Chilcoat, 1998) and combat intensity (Orcutt, Erickson, & Wolfe, 2004; Perconte, Wilson, Pontius, Dietrick, & Spiro, 1993) were associated with greater PTSD symptom severity, these constructs were included, along with participant age and test-retest interval, as covariates in the second regression step. Pre-deployment scores for the neurocognitive tests were entered in the third step.<sup>1</sup>

To examine post-deployment cross-sectional associations between PTSD symptom severity and neuropsychological functioning, a series of hierarchical linear regressions were specified with post-deployment PCL score as the outcome variables for the analyses. In the first block, we entered covariates of participant age, gender, self-reported combat intensity, and test-retest interval. In the second regression

<sup>1</sup> Cross-sectional studies have included IQ estimates as approximations of pre-exposure cognitive integrity. Because our study design included neuropsychological assessment both pre- and post-deployment, we did not include an IQ estimate as a covariate in our primary analyses. However, because previous research has found IQ estimates to be a significant predictor of PTSD status (e.g., Ozer et al., 2003), and for the purposes of comparison with the cross-sectional literature, we repeated our primary analyses with the NES3 Vocabulary test as a covariate. Results of these analyses showed that pre-deployment NES3 Vocabulary scores were not significantly associated with either post-deployment PCL summary scores,  $\beta = -0.08$ ,  $t(630) = -0.58$ ,  $p = .56$ , or with residualized post-deployment PCL summary scores,  $\beta = 0.03$ ,  $t(626) = 0.29$ ,  $p = .77$ . Furthermore, the inclusion of the Vocabulary scores as a covariate did not change the pattern of results.

block, we entered post-deployment performance scores for memory, response inhibition, working memory, and sustained attention.

## RESULTS

### Sample Characteristics

Table 1 presents pre-deployment characteristics of the final sample, as well as the characteristics of soldiers who participated at pre-deployment, but who were excluded or did not participate in Time 2 assessments. Participants in the final sample generally reflected the broader Operation Iraqi Freedom

(OIF)-deployed Army population. Women were slightly underrepresented. Although enlisted personnel constitute the majority of deployers, commissioned officers were also underrepresented. Nonparticipants at post-deployment assessment reported less sleep and were more likely to be women, officers, have had a previous overseas deployment, used nonpsychoactive medication, and reported a history of neuromedical disorder than participants in the final sample. These groups, however, did not differ in pre-deployment PCL summary scores or estimated PTSD screening rates (i.e., PCL scores of 50 or greater and endorsement of the requisite number of symptoms in each of the *DSM-IV* symptom clusters). Furthermore, the participant and nonparticipant

**Table 1.** Demographic and contextual sample characteristics at pre-deployment

Variable	Post-deployment Participants ( <i>n</i> = 668)	Post-deployment Non-Participants ( <i>n</i> = 287)	<i>p</i> value
Age (year), <i>M</i> ( <i>SD</i> )	25.04 (5.23)	25.03 (5.40)	.98
Ethnicity minority, no. (%)	292 (43.80)	133 (46.80)	.39
Women, no. (%)	55 (8.20)	49 (17.10)	<.0001
Education (year), <i>M</i> ( <i>SD</i> )	12.45 (1.25)	12.57 (1.67)	.28
Years in Army, <i>M</i> ( <i>SD</i> )	4.09 (4.23)	4.36 (4.72)	.39
Enlisted rank (enlisted), no. (%)	655 (98.10)	265 (93.30)	<.0001
Previous operational deployment, no. (%)	76 (11.40)	31 (28.70)	<.0001
Married, no. (%)	301 (45.10)	129 (45.60)	.90
Hours of sleep per night (past week), <i>M</i> ( <i>SD</i> )	5.92 (1.28)	5.71 (1.36)	.03
Alcoholic drinks consumed per week (past month), <i>M</i> ( <i>SD</i> )	8.14 (12.06)	8.43 (12.95)	.75
Current cigarette smokers, no. (%)	319 (47.80)	120 (42.30)	.12
Reported taking prescribed or over the counter medication (past 48 hr), no. (%)	218 (32.60)	113 (39.40)	.05
Reporting taking prescribed psychoactive or anticonvulsant medications (past 48 hr), no. (%)	13 (1.90)	8 (2.80)	.42
Reported developmental disorder, no. (%)	85 (12.80)	36 (12.70)	.99
Reported psychiatric disorder, no. (%)	41 (6.20)	27 (9.40)	.08
Reported past alcohol use disorder, no. (%)	28 (4.20)	16 (5.60)	.37
Reported prior head injury with loss of consciousness > 15 min, no. (%)	37 (5.60)	16 (5.70)	.94
Reported other neuromedical disorder, no. (%)	19 (2.90)	16 (5.90)	.03
Pre-deployment PCL, <i>M</i> ( <i>SD</i> )	29.18 (12.53)	30.85 (14.19)	.09
Pre-deployment PCL scores of 50 or more and endorsement of <i>DSM-IV</i> symptom clusters, no. (%)	56 (8.40)	28 (10.90)	.26
Pre-deployment WMS-III Verbal Paired Associates immediate recall, <i>M</i> ( <i>SD</i> )	1.93 (1.74)	1.80 (1.70)	.30
Pre-deployment WMS-III Verbal Paired Associates Retention, <i>M</i> ( <i>SD</i> )	89.53 (19.04)	88.93 (20.69)	.70
Pre-deployment WMS Visual Reproductions Immediate recall, <i>M</i> ( <i>SD</i> )	8.27 (2.11)	8.35 (2.35)	.60
Pre-deployment WMS Visual Reproductions Retention, <i>M</i> ( <i>SD</i> )	88.17 (15.78)	88.07 (15.74)	.92
Pre-deployment NES3 CPT log-transformed false positives, <i>M</i> ( <i>SD</i> )	0.54 (0.54)	0.52 (0.52)	.59
Pre-deployment NES3 CPT log-transformed negative responses, <i>M</i> ( <i>SD</i> )	0.29 (0.53)	0.24 (0.50)	.26
Pre-deployment Trail Making B – A (log-transformed seconds), <i>M</i> ( <i>SD</i> )	0.81 (0.32)	0.81 (0.28)	.96

*Note.* The sample size varies slightly across observations because of missing data. PCL = PTSD Checklist; WMS = Wechsler Memory Scale; WMS-III = Wechsler Memory Scale, 3rd edition; NES3 CPT = Neurobehavioral Evaluation System, 3rd edition, Continuous Performance Task.

groups did not differ on pre-deployment performances of memory, inhibition, working memory, and sustained attention.

Table 2 presents the means, standard deviations, and ranges for all continuous study variables among the participants. The standard deviation and range of the PCL scores and neurocognitive variables showed dispersion at each assessment. Inspection of the model residuals for the series of hierarchical regressions demonstrated normality and homoscedasticity.

Table 3 presents zero-order correlations computed among the variables of interest. Pre-deployment visual memory percent retention scores were significantly and negatively correlated with pre-deployment PCL scores; pre-deployment immediate visual memory scores were significantly and negatively correlated with post-deployment PCL scores. No other neuropsychological measures were correlated with either pre- or post-deployment PCL scores.

### Prospective Analyses

Table 4 presents results of the regressions that explored associations between pre-deployment neuropsychological performances and post-deployment residualized change in PTSD symptom levels. Approximately 33% of the variance in residualized PCL scores was accounted for by each of the models. In each of the final models, higher levels of pre-deployment PCL scores, female gender, and higher levels of combat intensity were significantly associated with higher levels of residualized post-deployment PCL scores. Visual

Reproductions immediate recall was the only pre-deployment neuropsychological performance indicator associated with residualized post-deployment PCL scores. The association was negative, suggesting that less proficient acquisition of visual information at pre-deployment was associated with less favorable PTSD outcomes at post-deployment.

Exploratory *post hoc* regressions were conducted to examine whether the influences of pre-deployment neurocognitive performances on residualized PCL scores post-deployment differed by level of pre-deployment PCL scores. Interaction terms representing the product of pre-deployment PCL scores and each pre-deployment neurocognitive performance indicator were tested at the final regression step in separate models. Pre-deployment PCL scores moderated the associations of pre-deployment verbal,  $\beta = -0.01$ ,  $t(626) = -2.14$ ,  $p < .03$ , and visual,  $\beta = -0.04$ ,  $t(626) = -2.52$ ,  $p < .02$ , immediate recall performances with residualized PCL scores post-deployment. Specifically, the associations between lower pre-deployment proficiency in verbal and visual information acquisition and higher residualized PCL scores post-deployment were stronger at higher levels of pre-deployment PTSD symptoms. Interaction terms for the remaining pre-deployment neurocognitive performances were nonsignificant.

### Cross-sectional Analyses

Table 5 presents the results of regression models that examined cross-sectional associations of post-deployment PCL summary scores with post-deployment neuropsychological

**Table 2.** Means, standard deviations, and ranges for PTSD symptoms and neurocognitive performance measures at pre- and post-deployment ( $N = 668$ )

Variable	Pre-deployment			Post-deployment		
	<i>M</i>	<i>SD</i>	Range	<i>M</i>	<i>SD</i>	Range
PCL summary score	29.12	12.35	17–67	32.40	13.21	17–72
Memory and Neurocognitive variables						
WMS-III Verbal Paired Associates, immediate recall, number correct, trials 1–4	18.43	7.11	0–32	20.01	7.32	1–32
WMS-III Verbal Paired Associates, percent retention	89.53	19.04	0–100	90.45	18.38	0–100
WMS Visual Reproductions, immediate recall	8.27	2.11	1.51–14	8.31	2.12	1.74–14
WMS Visual Reproductions, percent retention	88.17	15.78	7.28–100	88.51	15.21	12–100
Trail Making B – A, log-transformed seconds	0.81	0.32	–0.17–1.77	0.80	0.29	.03–1.67
NES3 CPT, log-transformed false positives score	0.54	0.54	0–2.16	0.53	0.57	0–2.27
NES3 CPT, log-transformed negative responses score	0.28	0.50	0–1.88	0.28	0.51	0–1.91
Covariates						
Age, in years (pre-deployment)	25.00	5.10	17.70–40.70			
DRRI, Combat Experiences Scale, summary score (post-deployment)				18.13	10.43	0–49.87
Test-retest interval, number of days				523.16	95.35	462–769

*Note.* PTSD = posttraumatic stress disorder; PCL = PTSD Checklist; WMS = Wechsler Memory Scale; WMS-3 = Wechsler Memory Scale, 3rd edition; NES3 CPT = Neurobehavioral Evaluation System, 3rd edition Continuous Performance Task; DRRI = Deployment Risk and Resilience Inventory.

**Table 3.** Correlations for PTSD and neurocognitive performance measures

Variable	1	2	3	4	5	6	7	8	9
1	1.00								
2	.49**	1.00							
3	-.03	-.06	1.00						
4	.02	-.03	.46**	1.00					
5	-.04	-.11**	.23**	.13**	1.00				
6	-.09*	-.05	.16**	.20**	.07	1.00			
7	.03	.00	-.05	-.06	-.06	-.05	1.00		
8	.073	-.02	-.08*	-.06	-.00	-.09*	.30**	1.00	
9	.07	.07	-.08*	-.09*	-.11**	.00	.06	-.03	1.00

*Note.*  $N = 668$ , \* $p < .05$ , \*\* $p < .01$ ; PTSD = posttraumatic stress disorder; 1 = PTSD Checklist pre-deployment; 2 = PTSD Checklist post-deployment; 3 = Wechsler Memory Scale-III, Verbal Paired Associates, immediate recall, number correct, trials 1–4; 4 = Wechsler Memory Scale-III Verbal Paired Associates, percent retention; 5 = Wechsler Memory Scale Visual Reproductions, immediate recall; 6 = Wechsler Memory Scale Visual Reproductions, percent retention; 7 = Neurobehavioral Evaluation System, 3rd edition, Continuous Performance Task, log-transformed false positives score; 8 = Neurobehavioral Evaluation System, 3rd edition, Continuous Performance Task, log-transformed negative responses score; 9 = Trail Making B – A (log-transformed seconds).

performances. Approximately 12–15% of the estimated variance in post-deployment PTSD symptoms was accounted for by each of the final models. Gender and combat intensity were positively correlated with post-deployment PCL summary scores, suggesting that female gender and higher levels of combat intensity were related to greater PTSD symptom severity following deployment. Both post-deployment verbal and visual immediate recall performances were significantly associated with post-deployment PTSD levels, such that lower capacity for verbal and visual information acquisition following deployment was associated with more post-deployment PTSD symptomatology.

## DISCUSSION

This study is the first to examine prospectively relationships between specific neurocognitive performances and the full range of PTSD symptoms after trauma exposure. Results showed that pre-trauma visual immediate memory performance was associated negatively with post-deployment PTSD symptom severity, even after controlling for pre-deployment PTSD symptom levels, combat intensity, test-retest interval, age, and gender. This finding suggests that the integrity of at least one component of visual memory may alter risk of PTSD symptom expression following exposure to extreme stress, contributing to variance in symptom outcomes above and beyond such potent factors as stressor severity (measured by combat intensity) and pre-existing symptom levels. Findings also cannot be attributed to age, gender, or the passage of time between the two assessments.

The finding of a relationship between pre-exposure visual immediate recall and post-deployment PTSD mirrors research documenting a link between Army entrance examination scores and subsequent PTSD (Gale et al., 2008; Kremen et al., 2007; Macklin et al., 1998; Thompson & Gottesman, 2008). It is also consistent with, but more circumscribed than, the prospective findings reported by Parslow and Jorm (2007), which showed that more proficient immediate and

delayed verbal recall, verbal working memory, visuo-motor speed, and verbal intelligence measured prior to exposure to a natural disaster were associated with lower post-trauma PTSD re-experiencing and arousal symptoms. Our test, however, was more conservative than Parslow and Jorm (2007), in that we were able to examine the relationship between baseline functioning and change in PTSD symptoms, allowing us to make firmer inferences about the direction of causation.

We found an association of post-deployment PTSD with memory when memory was measured in the visual-spatial, but not in the verbal-auditory, modality. Autobiographical memory studies of non-trauma-exposed samples have demonstrated that decreased visual input reduces the recollection of autobiographical events (Rubin, Burt, & Fifeld, 2003), and damage to the occipital lobe impedes autobiographical memory (Greenberg & Rubin, 2003). Although speculative, it is possible that the ability to form a visual image allows for rehearsal and appropriate habituation to the traumatic event. Thus, proficiency in the initial acquisition of visual images may promote visual processing of traumatic experiences necessary for habituation and subsequent resilience and/or recovery. This possibility is consistent with research showing that visual imagery evokes stronger affective responses than verbal processing (Holmes, Wilson, Pontius, Dietrick, & Spiro, 2006) and is more effective than verbal processing in reducing anxiety in the context of interpretation training (Holmes & Mathews, 2005). It is also consistent with Gilbertson and colleagues (Gilbertson et al., 2002; 2007), who showed that, in monozygotic Vietnam veteran twins discordant for combat exposure, smaller hippocampi and correlated deficiencies in solving allocentric (i.e., configural relationships among distal environmental features) visuo-spatial processing problems constituted a risk for the development of PTSD. As the hippocampus has been shown to be important in the processing of configural relationships in one's environment (Astur, Taylor, Mamelak, Philpott, & Sutherland, 2002) and configural processing of environmental



**Table 4.** Longitudinal associations of residualized PCL scores with pre-deployment neurocognitive performances

	B	SE B	$\beta$
Model A. Verbal and visual immediate recall			
Step 1 (Autoregressor)			
PCL summary score (pre-deployment)	0.51	0.04	.48***
Step 2 (Covariates)			
Age in years	0.16	0.09	.06
Gender	3.83	1.63	.08*
DRRI Combat Experiences Scale, summary score	0.35	0.04	.28***
Test-retest interval, number of days	-0.00	0.01	-.01
Step 3 (Pre-deployment neurocognitive performances)			
WMS-III Verbal Paired Associates, immediate recall, sum of trials A-D	-0.04	0.06	-.02
WMS Visual Reproductions, immediate recall	-0.45	0.21	-.07*
Trail Making B - A (log-transformed seconds)	0.28	1.37	.01
NES3 CPT log-transformed false positives	0.41	0.85	.02
NES3 CPT log-transformed non-responses	-1.61	0.93	-.06
Model B. Verbal and visual retention			
Step 1 (Autoregressor)			
PCL summary score (pre-deployment)	0.51	0.04	.48***
Step 2 (Covariates)			
Age in years	0.17	0.09	.07*
Gender	3.71	1.64	.08*
DRRI Combat Experiences Scale, summary score	0.36	0.04	.29***
Test-retest interval, number of days	0.00	0.01	-.00
Step 3 (Pre-deployment neurocognitive performances)			
WMS-III Verbal Paired Associates, percent retention	-0.02	0.02	-.03
WMS Visual Reproductions, percent retention	-0.03	0.03	-.03
Trail Making B - A (log-transformed seconds)	0.50	1.37	.01
NES3 CPT log-transformed false positives	0.45	0.85	.02
NES3 CPT log-transformed non-responses	-1.68	0.93	-.06

Note. For Model A: Step 1,  $R^2 = .24$ ,  $F(1, 636) = 205.71$ ,  $p < .00$ ; Step 2,  $\Delta R^2 = .08$ ,  $\Delta F(4, 632) = 17.99$ ,  $p < .00$ ;  $R^2 = .32$ ,  $F(5, 632) = 59.93$ ,  $p < .00$ ; Step 3,  $\Delta R^2 = .01$ ,  $\Delta F(5, 627) = 1.74$ ,  $p = .12$ ; final  $R^2 = .33$ ,  $F(10, 627) = 31.01$ ,  $p < .00$ . For Model B: Step 1,  $R^2 = .24$ ,  $F(1, 636) = 205.71$ ,  $p < .00$ ; Step 2,  $\Delta R^2 = .08$ ,  $\Delta F(4, 632) = 17.99$ ,  $p < .00$ ;  $R^2 = .32$ ,  $F(5, 632) = 59.93$ ,  $p < .00$ ; Step 3,  $\Delta R^2 = .01$ ,  $\Delta F(5, 627) = 1.13$ ,  $p = .35$ ; final  $R^2 = .33$ ,  $F(10, 627) = 30.56$ ,  $p < .00$ .

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$ .

$\beta$  = standardized parameter estimates; B = unstandardized parameter estimates; PCL = PTSD checklist; WMS = Wechsler Memory Scale; WMS-III = Wechsler Memory Scale, 3rd edition; NES3 CPT = Neurobehavioral Evaluation System, 3rd edition Continuous Performance Task. Parameter estimates are for the final model; DRRI = Deployment Risk and Resilience Inventory.

cues is pivotal in the extinction of conditioned fear responses (Frankland, Cestari, Filipkowski, McDonald, & Silva, 1998), Gilbertson et al. (2007) interpreted their findings to suggest that smaller hippocampal volume before trauma exposure might promote the development of PTSD through a failure to support visually-mediated context-appropriate extinction of conditioned emotional responses. Interestingly, dissociation, a potent risk factor for PTSD (e.g., Ozer, Best, Lipsey, & Weiss, 2003) involves alterations of the visual and somatosensory modalities (Bernstein & Putnam, 1986; Bremner et al., 1998). Regardless of the mechanism, the prospective results suggest that a pre-deployment neurocognitive strength (immediate visual memory, in particular) buffers against the adverse effects of deployment to a war-zone noted by other studies (Dohrenwend et al., 2006; Hoge et al., 2004, 2008; Kang, Natelson, Mahan, Lee, & Murphy, 2003).

Prior cross-sectional research showed relative performance deficiency on verbal memory (Brewin, Kleiner, Vasterling, & Field, 2007) and intellectual tasks (e.g.,

Vasterling et al., 1998) among those with PTSD. In contrast, our prospective findings indicated that a visual, but not a verbal, memory task was significantly associated with residualized post-deployment PCL scores. As demonstrated by Gilbertson et al. (2007) and prior research demonstrating PTSD-related dissociations between global and local processing on visuo-spatial tasks (c.f. Vasterling, Brailey, Sutker, 2000; Vasterling, Duke, Tomlin, Lowery, & Kaplan, 2004), it is likely that PTSD is associated with relative decrements in only select aspects of visuo-spatial processing that are not detected on all tasks. It is also probable that our measures of visual and verbal memory processes were not pure with respect to the processes invoked to complete the tasks. For example, geometric line drawings may be verbally elaborated, and verbal word pairs may be visualized. Inclusion of verbal and visual memory indices in each of the regression analyses permitted some control for overlapping processes; however, because we only included one test representative of each modality, and the two memory tests also varied on

**Table 5.** Cross-sectional associations of post-deployment PCL scores with post-deployment neurocognitive performances

	B	SE B	$\beta$
Model A. Verbal and visual immediate recall			
Step 1 (Covariates)			
Age in years	0.01	0.10	.00
Gender	7.37	1.80	.16***
DRRI Combat Experiences Scale, summary score	0.41	0.05	.32***
Test-retest interval, number of days	-0.01	0.01	-.03
Step 2 (Post-deployment neurocognitive performances)			
WMS-III Verbal Paired Associates, immediate recall, sum of trials 1-4	-0.16	0.07	-.09*
WMS Visual Reproductions, immediate recall	-0.91	0.24	-.15***
Trail Making B - A (log-transformed seconds)	0.43	1.67	.01
NES3 CPT log-transformed false positives	0.12	0.91	.01
NES3 CPT log-transformed non-responses	1.19	1.04	.05
Model B. Verbal and visual retention			
Step 1 (Covariates)			
Age in years	0.08	0.10	.03
Gender	7.19	1.83	.15
DRRI Combat Experiences Scale, summary score	0.40	0.05	.32
Test-retest interval, number of days	-0.00	0.01	-.03
Step 2 (Post-deployment neurocognitive performances)			
WMS-III Verbal Paired Associates, percent retention	-0.01	0.03	-.01
WMS Visual Reproductions, percent retention	-0.06	0.03	-.06
Trail Making B - A (log-transformed seconds)	1.09	1.69	.02
NES3 CPT log-transformed false positives	0.21	0.92	.01
NES3 CPT log-transformed non-responses	1.64	1.04	.06

Note. For Model A: Step 1,  $R^2 = .11$ ,  $F(4, 645) = 19.24$ ,  $p < .00$ ; for Step 2,  $\Delta R^2 = .04$ ,  $\Delta F(5, 640) = 5.89$ ,  $p < .00$ ; final  $R^2 = .15$ ,  $F(9, 640) = 12.15$ ,  $p < .00$ . For Model B: Step 1,  $R^2 = .11$ ,  $F(4, 643) = 19.66$ ,  $p < .00$ ; for Step 2,  $\Delta R^2 = .01$ ,  $\Delta F(5, 638) = 1.41$ ,  $p = .22$ ; final  $R^2 = .12$ ,  $F(9, 638) = 9.55$ ,  $p < .00$ .

\* $p < .05$ , \*\* $p < .01$ , \*\*\* $p < .001$ .

$\beta$  = standardized parameter estimates; B = unstandardized parameter estimates; PCL = PTSD checklist; WMS = Wechsler Memory Scale; WMS-III = Wechsler Memory Scale, 3rd edition; NES3 CPT = Neurobehavioral Evaluation System, 3rd edition Continuous Performance Task. Parameter estimates are for the final model; DRRI = Deployment Risk and Resilience Inventory.

attributes other than modality, modality-specific interpretations of our findings should be made with caution.

*Post hoc* analyses revealed that the effects of pre-deployment levels of immediate verbal and visual memory on post-deployment PTSD symptom levels were moderated by pre-deployment PTSD symptom levels. At higher levels of pre-deployment PTSD symptoms, neurocognitive performance exerted a greater influence on post-deployment PTSD symptom levels, as demonstrated both by increased strength of associations and by a broader scope of associations (i.e., visual and verbal learning). Previous studies have shown that pre-existing psychopathology increases risk for PTSD following exposure to a traumatic event (Bowman, 1997; Brewin, Andrews, & Valentine, 2000; Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; Kessler et al., 1999; Ozer et al., 2003; Schlenger et al., 1992). The observation that pre-exposure psychopathology interacted with a pre-exposure neurocognitive factor represents an intriguing finding, suggesting that intact neurocognitive skills may be particularly important in facilitating successful coping with pre-existing psychological distress in the face of cumulative stress exposures.

The finding that immediate recall, but not retention, of verbal and visual-spatial information was associated with post-deployment PTSD symptoms raises the question of whether attention or strategic memory processes impacting initial registration of information are particularly important to psychological resilience and recovery following trauma exposure. Although we did not document an association with pre-deployment attentional or executive measures and post-deployment PTSD symptom change, this assertion is consistent with neuropsychological conceptualizations of PTSD that emphasize the role of the prefrontal cortex (e.g., Carrion et al., 2001; De Bellis et al., 2002; Karl et al., 2006; Rauch et al., 1996; Shin et al., 2004) and prior cross-sectional work (e.g., Isaac, Cushway, & Jones, 2006; Jenkins, Langlais, Delis, & Cohen, 1998; Uddo et al., 1993; Vasterling et al., 1998, 2002; Yehuda et al., 1995; Yehuda, Golier, Halligan, & Harvey, 2004) documenting PTSD-related impairment of memory processes (e.g., sensitivity to interference) linked to frontal lobe integrity. Alternatively, the association with visual immediate recall and PTSD symptoms could reflect the contribution of primary visual-spatial processing deficits to PTSD risk. Because we did not include a task of visual-spatial processing without a memory component, however,

the degree to which primary visual-spatial *versus* visual-spatial memory processing accounts for the relationship between visual immediate memory and PTSD symptoms remains unclear.

As an extension of the previous literature, we also examined the cross-sectional relationships of neurocognitive performances to PTSD symptom severity at post-deployment and found that immediate visual recall and verbal learning performances were negatively correlated with PTSD symptom severity. These findings are consistent with the cross-sectional literature, revealing both visual and verbal memory associations with PTSD symptoms (Brewin et al., 2007), but do not directly address causal direction. However, in the absence of a longitudinal relationship between pre-exposure verbal learning and post-deployment PTSD symptoms (except when PTSD symptoms were already high at baseline), the post-deployment relationship of verbal learning to PTSD symptoms raises the question of whether PTSD may have led to a decline in verbal learning. This assertion is consistent with Parslow and Jorm (2007)'s finding of an interaction between time (pre- vs. post-trauma) and post-trauma PTSD on a word recall task. It may be that some cognitive weaknesses confer risk of PTSD development, whereas others are a result of PTSD.

There may be alternative explanations for the findings. For example, it could be argued that pre-deployment visual memory decrements are associated with baseline PTSD symptoms, and that the association between pre-deployment visual memory and post-deployment PCL scores simply reflects elevated baseline PCL scores. However, the correlation between pre-deployment immediate visual memory and pre-deployment PCL scores was not significant, and baseline PCL scores are parceled out of post-deployment PCL scores, via their inclusion in the models as a covariate. Another possibility is that the visual immediate memory test was particularly sensitive to insufficient effort or symptom exaggeration. If so, symptom feigning would be reflected by both poorer performance on the visual immediate memory test and elevated PCL scores. However, we excluded participants for insufficient effort based on their TOMM responses, and there is no evidence that visual immediate memory is more sensitive to insufficient effort/symptom exaggeration than other neuropsychological tasks administered.

There are several limitations to our study. We included only one measure of each of the neuropsychological constructs of interest, limiting the extent to which findings can be generalized beyond the specific parameters of the tasks administered. As discussed earlier, we did not include a control test of visual-spatial processing devoid of a memory component. The verbal and visual memory tasks were also not well-matched with respect to the specific task demands. Thus, we remain unable to exclude the possibility that specific task demands accounted for the dissociation of findings between verbal and visual immediate recall tasks.

The study design offered the advantage of allowing examination of the relationship between pre-trauma memory functioning and post-trauma PTSD symptoms prior to the

PTSD becoming chronic. It will be beneficial, however, to conduct longer-term longitudinal studies in which the relationship between memory and PTSD symptoms is examined over time, permitting determination of whether pre-trauma memory is equally potent at all time points in the natural history of PTSD. Such an approach is consistent with previous findings showing that risk factors associated with developing PTSD may differ from risk factors associated with maintaining PTSD (Dunmore, Clark, & Ehlers, 1999; Koenen, Stellman, Stellman, & Sommer, 2003; Schnurr, Lunney, & Sengupta, 2004).

Brewin et al. (2000) showed that sample type (i.e., civilian vs. military) may moderate the associations between risk factors and PTSD, with effects generally being stronger for military samples. Because our sample was comprised of active duty military personnel exposed to war-zone trauma, the extent to which results will generalize to nonmilitary trauma populations is unknown. Importantly, many of the individuals in our sample were not trauma naïve or free of PTSD symptoms prior to deployment. However, an advantage of the longitudinal design is that we were able to control statistically for pre-deployment symptom levels. Despite these limitations, the longitudinal design, performance-based neuropsychological measures, and a sizable sample of deployed participants provide unique information regarding the longitudinal trajectory of the relationship between baseline neuropsychological performance and PTSD symptom outcome following exposure to extreme stress.

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## REFERENCES

- American Psychiatric Association. (1994). *Diagnostic and statistical manual of mental disorders* (4<sup>th</sup> ed.). Washington, DC: Author.
- Arnsten, A.F.T., & Goldman-Rakic, P.S. (1998). Noise stress impairs prefrontal cortical cognitive function in monkeys: Evidence for a hyperdopaminergic mechanism. *Archives of General Psychiatry*, 55(4), 362–368.



- Astur, R.S., Taylor, L.B., Mamelak, A.N., Philpott, L., & Sutherland, R.J. (2002). Humans with hippocampus damage display severe spatial memory impairments in a virtual Morris water task. *Behavior and Brain Research*, 132(1), 77–84.
- Bernstein, E.M., & Putnam, F.W. (1986). Development, reliability, and validity of a dissociation scale. *Journal of Nervous and Mental Disease*, 174(12), 727–735.
- Birnbaum, S., Gobeske, K.T., Auerbach, J., Taylor, J.R., & Arnsten, A.F.T. (1999). A role for norepinephrine in stress-induced cognitive deficits:  $\alpha$ -1-Adrenoceptor mediation in the prefrontal cortex. *Biological Psychiatry*, 46(9), 1266–1274.
- Blake, D.D., Keane, T.M., Wine, P.R., & Mora, C. (1990). Prevalence of PTSD symptoms in combat veterans seeking medical treatment. *Journal of Traumatic Stress*, 3(1), 15–27.
- Blanchard, E.B., Jones-Alexander, J., Buckley, T.C., & Forneris, C.A. (1996). Psychometric properties of the PTSD Checklist (PCL). *Behaviour Research and Therapy*, 34(8), 669–673.
- Bonne, O., Grillon, C., Vythilingam, M., Neumeister, A., & Charney, D.S. (2004). Adaptive and maladaptive psychobiological responses to severe psychological stress: Implications for the discovery of novel pharmacotherapy. *Neuroscience and Biobehavioral Reviews*, 28(1), 65–94.
- Bowman, M.L. (1997). *Individual differences in posttraumatic response: Problems with the adversity-distress connection*. Mahwah, NJ: Erlbaum.
- Bremner, J.D., Innis, R.B., Southwick, S.M., Staib, L., Zoghbi, S., & Charney, D.S. (2000). Decreased benzodiazepine receptor binding in prefrontal cortex in combat-related posttraumatic stress disorder. *American Journal of Psychiatry*, 157(7), 1120–1126.
- Bremner, J.D., Krystal, J.H., Putnam, F., Southwick, S.M., Marmar, C., & Charney, D.S. (1998). Measurement of dissociative states with the Clinician Administered Dissociative States Scale (CADSS). *Journal of Traumatic Stress*, 11(1), 125–136.
- Breslau, N., Kessler, R.C., & Chilcoat, H.D. (1998). Trauma and posttraumatic stress disorder in the community: The 1996 Detroit Area Survey of Trauma. *Archives of General Psychiatry*, 55(7), 626–632.
- Brewin, C.R. (2008). What is it that a neurobiological model of PTSD must explain? *Progress in Brain Research*, 167, 217–228.
- Brewin, C.R., Andrews, B., & Valentine, J.D. (2000). Meta-analysis of risk factors for posttraumatic stress disorder in trauma-exposed adults. *Journal of Consulting and Clinical Psychology*, 68(5), 748–766.
- Brewin, C.R., Kleiner, J.S., Vasterling, J.J., & Field, A.P. (2007). Memory for emotionally neutral information in posttraumatic stress disorder: A meta-analytic investigation. *Journal of Abnormal Psychology*, 116(3), 448–463.
- Carrion, V.G., Weems, C.F., Eliez, S., Patwardhan, A., Brown, W., Ray, R.D., & Reiss, A.L. (2001). Attenuation of frontal asymmetry in pediatric posttraumatic stress disorder. *Biological Psychiatry*, 50(12), 943–951.
- Constans, J.I., McCloskey, M.S., Vasterling, J.J., Brailey, K., & Mathews, A. (2004). Suppression of attentional bias in PTSD. *Journal of Abnormal Psychology*, 113(2), 315–323.
- Dalglish, T., Taghavi, R., Neshat-Doost, H., Moradi, A., Canterbury, R., & Yule, W. (2003). Patterns of processing bias for emotional information across clinical disorders: A comparison of attention, memory, and prospective cognition in children and adolescents with depression, generalized anxiety, and post-traumatic stress disorder. *Journal of Clinical Child and Adolescent Psychology*, 32(1), 10–21.
- De Bellis, M.D., Keshavan, M.S., Shifflett, H., Iyengar, S., Beers, S.R., Hall, J., & Moritz, G. (2002). Brain structures in pediatric maltreatment-related posttraumatic stress disorder: A sociodemographically matched study. *Biological Psychiatry*, 52(11), 1066–1078.
- Dohrenwend, B.P., Turner, J.B., Turse, N.A., Adams, B.G., Koenen, K.C., & Marshall, R. (2006). The psychological risks of Vietnam for U.S. veterans: A revisit with new data and methods. *Science*, 313(5789), 979–982.
- Dunmore, E., Clark, D.M., & Ehlers, A. (1999). Cognitive factors involved in the onset and maintenance of posttraumatic stress disorder (PTSD) after physical or sexual assault. *Behaviour Research and Therapy*, 37(9), 809–829.
- Ehlers, A., & Clark, D. (2000). A cognitive model of posttraumatic stress disorder. *Behaviour Research and Therapy*, 38(4), 319–345.
- Foa, E.B., Feske, U., Murdock, T.B., Kozak, M.J., & McCarthy, P.R. (1991). Processing of threat-related information in rape victims. *Journal of Abnormal Psychology*, 100(2), 156–162.
- Foa, E.B., & Jaycox, L.H. (1999). Cognitive-behavioral theory and treatment of posttraumatic stress disorder. In D. Spiegel (Ed.), *Efficacy and cost-effectiveness of psychotherapy* (pp. 23–61). Arlington, VA: American Psychiatric Publishing.
- Foa, E.B., & Riggs, D.S. (1994). Posttraumatic stress disorder and rape. In R. Pynoos (Ed.), *Posttraumatic stress disorder: A clinical review* (pp. 133–163). Baltimore, MD: Sidran Press.
- Forbes, D., Creamer, M., & Biddle, D. (2001). The validity of the PTSD checklist as a measure of symptomatic change in combat-related PTSD. *Behaviour Research and Therapy*, 39(8), 977–986.
- Frankland, P.W., Cestari, V., Filipkowski, R.K., McDonald, R.J., & Silva, A.J. (1998). The dorsal hippocampus is essential for context discrimination but not for contextual conditioning. *Behavioral Neuroscience*, 112(4), 863–874.
- Gale, C.R., Deary, I.J., Boyle, S.H., Barefoot, J., Mortensen, L.H., & Batty, G.D. (2008). Cognitive ability in early adulthood and risk of five specific psychiatric disorders in middle age: The Vietnam experience study. *Archives of General Psychiatry*, 65(12), 1410–1418.
- Gilbertson, M.W., Gurvits, T.V., Lasko, N.B., Orr, S.P., & Pitman, R.K. (2001). Multivariate assessment of explicit memory function in combat veterans with posttraumatic stress disorder. *Journal of Traumatic Stress*, 14(2), 413–431.
- Gilbertson, M.W., Paulus, L.A., Williston, S.K., Gurvits, T.V., Lasko, N.B., Pitman, R.K., & Orr, S.P. (2006). Neurocognitive function in monozygotic twins discordant for combat exposure: Relationship to posttraumatic stress disorder. *Journal of Abnormal Psychology*, 115(3), 484–495.
- Gilbertson, M.W., Shenton, M.E., Ciszewski, A., Kasai, K., Lasko, N.B., Orr, S.P., & Pitman, R.K. (2002). Smaller hippocampal volume predicts pathologic vulnerability to psychological trauma. *Nature Neuroscience*, 5(11), 1242–1247.
- Gilbertson, M.W., Williston, S.K., Paulus, L.A., Lasko, N.B., Gurvits, T.V., Shenton, M.E., & Orr, S.P. (2007). Configural cue performance in identical twins discordant for posttraumatic stress disorder: Theoretical implications for the role of hippocampal function. *Biological Psychiatry*, 62(5), 513–520.
- Greenberg, D.L., & Rubin, D.C. (2003). The neuropsychology of autobiographical memory. *Cortex*, 39(4–5), 687–728.
- Hoge, C.W., Castro, C.A., Messer, S.C., McGurk, D., Cotting, D.I., & Koffman, R.L. (2004). Combat duty in Iraq and Afghanistan, mental health problems, and barriers to care. *New England Journal of Medicine*, 351(1), 13–22.



- Hoge, C.W., McGurk, D., Thomas, J.L., Cox, A.L., Engel, C.C., & Castro, C.A. (2008). Mild traumatic brain injury in U.S. Soldiers returning from Iraq. *New England Journal of Medicine*, 358(5), 453–463.
- Holmes, E.A., & Mathews, A. (2005). Mental imagery and emotion: A special relationship? *Emotion*, 5(4), 489–497.
- Holmes, E.A., Mathews, A., Dalgleish, T., & Mackintosh, B. (2006). Positive interpretation training: Effects of mental imagery versus verbal training on positive mood. *Behavior Therapy*, 37(3), 237–247.
- Isaac, C.L., Cushway, D., & Jones, G.V. (2006). Is posttraumatic stress disorder associated with specific deficits in episodic memory? *Clinical Psychology Review*, 26(8), 939–955.
- Jelinek, L., Jacobsen, D., & Kellner, M. (2006). Verbal and nonverbal memory functioning in posttraumatic stress disorder. *Journal of Clinical and Experimental Neuropsychology*, 28(6), 940–948.
- Jenkins, M.A., Langlais, P.J., Delis, D., & Cohen, R. (1998). Learning and memory in rape victims with posttraumatic stress disorder. *American Journal of Psychiatry*, 155(2), 278–279.
- Jenkins, M.A., Langlais, P.J., Delis, D., & Cohen, R.A. (2000). Attentional dysfunction associated with posttraumatic stress disorder among rape survivors. *Clinical Neuropsychologist*, 14(1), 7–12.
- Kang, H.K., Natelson, B.H., Mahan, C.M., Lee, K.Y., & Murphy, F.M. (2003). Post-traumatic stress disorder and chronic fatigue syndrome-like illness among Gulf War veterans: A population-based survey of 30,000 veterans. *American Journal of Epidemiology*, 157(2), 141–148.
- Karl, A., Schaefer, M., Malta, L.S., Dorfel, D., Rohleder, N., & Werner, A. (2006). A meta-analysis of structural brain abnormalities in PTSD. *Neuroscience and Biobehavioral Reviews*, 30(7), 1004–1031.
- Kessler, R.C., Sonnega, A., Bromet, E., Hughes, M., & Nelson, C.B. (1995). Posttraumatic stress disorder in the National Comorbidity Survey. *Archives of General Psychiatry*, 52(12), 1048–1060.
- Kessler, R.C., Sonnega, A., Bromet, E., Hughes, M., Nelson, C.B., & Breslau, N. (1999). Epidemiological risk factors for trauma and PTSD. In R. Yehuda (Ed.), *Risk factors for posttraumatic stress disorder* (pp. 23–59). Washington, DC: American Psychiatric Association.
- King, D.W., King, L.A., & Vogt, D.S. (2003). *Manual for the Deployment Risk and Resilience Inventory (DRRI): A collection of measures for studying deployment-related experiences in military veterans*. Boston, MA: National Center for PTSD.
- King, L.A., King, D.W., Vogt, D.S., Knight, J., & Samper, R.E. (2006). Deployment Risk and Resilience Inventory: A collection of measures for studying deployment-related experiences of military personnel and veterans. *Military Psychology*, 18(2), 89–120.
- Koenen, K.C., Driver, K.L., Oscar-Berman, M., Wolfe, J., Folsom, S., Huang, M.T., & Schlesinger, L. (2001). Measures of prefrontal system dysfunction in posttraumatic stress disorder. *Brain and Cognition*, 45(1), 64–78.
- Koenen, K.C., Stellman, J.M., Stellman, S.D., & Sommer, J.F. (2003). Risk factors for course of posttraumatic stress disorder among Vietnam veterans: A 14-year follow-up of American Legionnaires. *Journal of Consulting and Clinical Psychology*, 71(6), 980–986.
- Kremen, W.S., Koenen, K.C., Boake, C., Purcell, S., Eisen, S.A., Franz, C.E., et al. (2007). Pretrauma cognitive ability and risk for posttraumatic stress disorder. *Archives of General Psychiatry*, 64(3), 361–368.
- Leskin, L.P., & White, P.M. (2007). Attentional networks reveal executive function deficits in posttraumatic stress disorder. *Neuropsychology*, 21(3), 275–284.
- Letz, R. (2000). *NES3 user's manual*. Atlanta, GA: Neurobehavioral Systems, Inc.
- Macklin, M.L., Metzger, L.J., Litz, B.T., McNally, R.J., Lasko, N.B., Orr, S.P., & Pitman, R.K. (1998). Lower precombat intelligence is a risk factor for posttraumatic stress disorder. *Journal of Consulting and Clinical Psychology*, 66(2), 323–326.
- McFarlane, A.C., Weber, D.L., & Clark, C.R. (1993). Abnormal stimulus processing in posttraumatic stress disorder. *Biological Psychiatry*, 34(5), 311–320.
- McNally, R.J., Kaspi, S.P., Riemann, B.C., & Zeitlin, S.B. (1990). Selective processing of threat cues in posttraumatic stress disorder. *Journal of Abnormal Psychology*, 99(4), 398–402.
- McNally, R.J., Lasko, N.B., Macklin, M.L., & Pitman, R.K. (1995). Autobiographical memory disturbance in combat-related posttraumatic stress disorder. *Behaviour Research and Therapy*, 33(6), 619–630.
- O'Bryant, S.E., Engel, L.R., Kleiner, J.S., Vasterling, J.J., & Black, F.W. (2007). Test of memory malingering (TOMM) trial 1 as a screening measure for insufficient effort. *Clinical Neuropsychologist*, 21(3), 511–521.
- Ohl, F., Michaelis, T., Vollmann-Honsdorf, G.K., Kirschbaum, C., & Fuchs, E. (2000). Effect of chronic psychosocial stress and long-term cortisol treatment on hippocampus-mediated memory and hippocampal volume: A pilot-study in tree shrews. *Psychoneuroendocrinology*, 25(4), 357–363.
- Orcutt, H.K., Erickson, D.J., & Wolfe, J. (2004). The course of PTSD symptoms among Gulf War veterans: A growth mixture modeling approach. *Journal of Traumatic Stress*, 17(3), 195–202.
- Ozer, E.J., Best, S.R., Lipsey, T.L., & Weiss, D.S. (2003). Predictors of posttraumatic stress disorder and symptoms in adults: A meta-analysis. *Psychological Bulletin*, 129(1), 52–73.
- Parslow, R.A., & Jorm, A.F. (2007). Pretrauma and posttrauma neurocognitive functioning and PTSD symptoms in a community sample of young adults. *American Journal of Psychiatry*, 164(3), 509–515.
- Perconte, S.T., Wilson, A.T., Pontius, E.B., Dietrick, A.L., & Spiro, K.J. (1993). Psychological and war stress symptoms among deployed and non-deployed reservists following the Persian Gulf War. *Military Medicine*, 158(8), 516–521.
- Rasmusson, A.M., Vythilingam, M., & Morgan, C.A. (2003). The neuroendocrinology of posttraumatic stress disorder: New directions. *CNS Spectrums*, 8(9), 651–667.
- Rauch, S.L., van der Kolk, B.A., Fisler, R.E., Alpert, N.M., Orr, S.P., Savage, C.R., et al. (1996). A symptom provocation study of posttraumatic stress disorder using positron emission tomography and script-driven imagery. *Archives of General Psychiatry*, 53(5), 380–387.
- Reitan, R.M. (1958). Validity of the Trail Making Test as an indicator of organic brain damage. *Perceptual and Motor Skills*, 8, 271–276.
- Rubin, D.C., Burt, C.D.B., & Fifeld, S.J. (2003). Experimental manipulations of the phenomenology of memory. *Memory and Cognition*, 31(6), 877–886.
- Ruggiero, K.J., Del Ben, K., Scotti, J.R., & Rabalais, A.E. (2003). Psychometric properties of the PTSD Checklist-Civilian Version. *Journal of Traumatic Stress*, 16(5), 495–502.

- Schlenger, W.E., Kulka, R.A., Fairbank, J.A., Hough, R.L., Jordan, B.K., Marmar, C.R., & Weiss, D.S. (1992). The prevalence of post-traumatic stress disorder in the Vietnam generation: A multimethod, multisource assessment of psychiatric disorder. *Journal of Traumatic Stress, 5*(3), 333–363.
- Schnurr, P.P., Lunney, C.A., & Sengupta, A. (2004). Risk factors for the development versus maintenance of posttraumatic stress disorder. *Journal of Traumatic Stress, 17*(2), 85–95.
- Shansky, R.M., Glavis-Bloom, C., Lerman, D., McRae, P., Benson, C., Miller, K., et al. (2004). Estrogen mediates sex differences in stress-induced prefrontal cortex dysfunction. *Molecular Psychiatry, 9*(5), 531–538.
- Shin, L.M., Orr, S.P., Carson, M.A., Rauch, S.L., Macklin, M.L., Lasko, N.B., et al. (2004). Regional cerebral blood flow in the amygdala and medial prefrontal cortex during traumatic imagery in male and female Vietnam veterans with PTSD. *Archives of General Psychiatry, 61*(2), 168–176.
- Southwick, S.M., Rasmusson, A., Barron, J., & Arnsten, A. (2005). Neurobiological and neurocognitive alterations and PTSD: A focus on norepinephrine, serotonin, and the HPA axis. In J.J. Vasterling & C.R. Brewin (Eds.), *The neuropsychology of PTSD: Biological, cognitive, and clinical perspectives*. New York: Guilford Press.
- Thompson, W.W., & Gottesman, I.I. (2008). Challenging the conclusion that lower preinduction cognitive ability increases risk for combat-related post-traumatic stress disorder in 2,375 combat-exposed, Vietnam War veterans. *Military Medicine, 173*(6), 576–582.
- Tombaugh, T.N. (1997). The Test of Memory Malinger (TOMM): Normative data from cognitively intact and cognitively impaired individuals. *Psychological Assessment, 9*(3), 260–268.
- Uddo, M., Vasterling, J.J., Brailey, K., & Sutker, P.B. (1993). Memory and attention in combat-related post-traumatic stress disorder (PTSD). *Journal of Psychopathology and Behavioral Assessment, 15*(1), 43–52.
- Vasterling, J.J., & Brailey, K. (2005). Neuropsychological findings in adults with PTSD. In J.J. Vasterling & C.R. Brewin (Eds.), *Neuropsychology of PTSD: Biological, cognitive, and clinical perspectives* (pp. 178–207). New York: Guilford Press.
- Vasterling, J.J., Brailey, K., Constans, J.I., & Sutker, P.B. (1998). Attention and memory dysfunction in posttraumatic stress disorder. *Neuropsychology, 12*(1), 125–133.
- Vasterling, J.J., Brailey, K., & Sutker, P.B. (2000). Olfactory identification in combat-related posttraumatic stress disorder. *Journal of Traumatic Stress, 13*(2), 241–253.
- Vasterling, J.J., Duke, L.M., Brailey, K., Constans, J.I., Allain, A.N., & Sutker, P.B. (2002). Attention, learning, and memory performances and intellectual resources in Vietnam veterans: PTSD and no disorder comparisons. *Neuropsychology, 16*(1), 5–14.
- Vasterling, J.J., Duke, L.M., Tomlin, H., Lowery, N., & Kaplan, E. (2004). Global-local visual processing in posttraumatic stress disorder. *Journal of the International Neuropsychological Society, 10*(5), 709–718.
- Vasterling, J.J., Proctor, S.P., Amoroso, P., Kane, R., Gackstetter, G., Ryan, M.A.K., & Friedman, M.J. (2006a). The Neurocognition Deployment Health Study: A prospective cohort study of Army soldiers. *Military Medicine, 171*(3), 253–260.
- Vasterling, J.J., Proctor, S.P., Amoroso, P., Kane, R., Heeren, T., & White, R.F. (2006b). Neuropsychological outcomes of Army personnel following deployment to the Iraq War. *Journal of the American Medical Association (JAMA), 296*(5), 519–529.
- Weathers, F., Litz, B.T., Herman, D.S., Huska, J.A., & Keane, T.M. (1993, November). The PTSD Checklist (PCL): Reliability, validity, and diagnostic utility. Paper presented at the Ninth Annual Meeting of the International Society for Traumatic Stress Studies, San Antonio, TX.
- Wechsler, D. (1945). A standardized memory scale for clinical use. *Journal of Psychology, 19*, 87–95.
- Wechsler, D. (1997). *Wechsler Memory Scale* (3rd ed.). San Antonio, TX: The Psychological Corporation.
- Yehuda, R. (2002). Current status of cortisol findings in post-traumatic stress disorder. *Psychiatric Clinics of North America, 25*(2), 341–368.
- Yehuda, R., Golier, J.A., Halligan, S.L., & Harvey, P.D. (2004). Learning and memory in Holocaust survivors with posttraumatic stress disorder. *Biological Psychiatry, 55*(3), 291–295.
- Yehuda, R., Keefe, R.S., Harvey, P.D., Levengood, R.A., Gerber, D.K., Geni, J., & Siever, L.J. (1995). Learning and memory in combat veterans with posttraumatic stress disorder. *American Journal of Psychiatry, 152*(1), 137–139.